

### **Remarks**

Claims 1-14 are pending. All of the pending claims have been rejected. Applicants address each of the Examiner rejections below. Applicants respectfully request reconsideration of the claims.

#### **§ 102 Rejections**

##### *Rejection of Claims 1, 8, 10 and 12*

Claims 1, 8, 10, and 12 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Moore et al. (U.S. Patent No. 6,224,832). The Examiner asserts that Moore discloses all of the elements of the claimed invention. Applicants respectfully traverse this rejection.

Moore describes a multi-reactor synthesizer that includes a set of reactor cells, each cell having an inlet and an outlet, pumping means for producing separate flow of plural reagents, and means for interconnecting the reactor cells. (Col. 2, lines 60-67) The reactor cells comprise a cylindrical cartridge that contains an inert supporting medium for immobilizing the compounds to be synthesized. (Col. 4, lines 10-14) The reactor modules of the Moore system are rearranged for each different step of a run, which requires the compounds to be anchored within a reactor so that they can be moved with each module to the next stage. (Col. 5, lines 14-35)

In contrast, the present claims recite a method for making a combinatorial library using a plug flow reactor, which is different from the anchored solid-phase synthesis type of system employed by Moore. In a plug flow reactor, a particular selected plug of material travels through the reactor with minimal axial mixing with an adjacent plug of material, even though there will be radial mixing within the plug. Such a system allows for the members of the combinatorial library to be separated in time as they exit the reactor. Moore does not describe the use of a “plug flow reactor” as is recited in the present claims. In the Moore system, the components of the library are all created at the same time and are separated in space as they are anchored to the reactor. The Moore system, therefore, would not be capable of plug flow operation.

Since Moore fails to disclose all of the elements of the claimed invention, the § 102 rejection based on Moore should be withdrawn. See *Verdegaal Bros. v. Union Oil Co. of*

*California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (A patent claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference.)

*Rejection of claim 1-4 and 8-13*

Claims 1-4 and 8-13 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Freitag (U.S. Patent No. 6,566,461). The Examiner asserts that Freitag discloses all of the elements of the claimed invention. Applicants respectfully traverse this rejection.

Freitag describes an apparatus for performing multiple chemical reactions in parallel. (Col. 4, lines 66-67) Each of the reactions is contained within separate reactor vessels, which are combined into a reactor block. (Col. 5, lines 13-55) Reactants to be added during a reaction are kept in a header barrel, which has a plunger to feed reactants from the header barrel through a transfer line into the reactor vessel. (Col. 5, lines 56-60)

As with Moore, discussed above, Freitag describes a reactor system in which the products are separated in space rather than time. Freitag fails to describe a plug flow mode of operation for the reactor, as is recited in the present claims. Freitag teaches that the reactor vessels are sealed (see e.g., claim 1) for a constant volume reaction. (Col. 6, lines 5-12) A sealed reactor vessel precludes the use of a plug flow system. In a plug flow reactor, there is ideally a continuous fluid flow through the system with minimal axial mixing. Such operation would not be possible with a sealed reaction vessel. Although Freitag teaches that the reactor may be configured to perform “semi-continuous or continuous” processes, these embodiments of the Freitag reactor do not operate in a plug flow manner. In column 20, Freitag describes the semi-continuous and continuous modes of operation, which are more akin to a Continuous Stirred Tank Reactor as opposed to a plug flow reactor. There is no teaching in Freitag of minimal axial mixing or any of the other conditions characteristic of a plug flow reactor.

Since Freitag fails to disclose a plug flow reactor as recited in the claims, the § 102 rejection based on Freitag should be withdrawn.

*Rejection of claims 1-3, 8-10, and 12*

Claims 1-3, 8-10, and 12 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Flanagan et al (2003/0055295). The Examiner asserts that all of the elements of the claimed invention can be found in the Flanagan reference. Applicants respectfully traverse this rejection.

Flanagan describes a method for performing multiple chemical reactions for rapid combinatorial screening of chemicals, catalysts, reactions, and associated process conditions (¶ 00160). The method involves providing an array of reactor vessels and reactants; loading each reactor vessel with at least one reactant; and allowing the reactions to proceed for a predetermined time interval. This system, referred to as an Incremental Flow Reactor (IFR), is able to simulate on a micro-scale the types of chemical reactions that are carried out in production-scale Continuous Stirred Tank Reactors (CSTRs). Specifically, Flanagan states:

It is evident that the behavior of the present incremental flow method approaches that of a continuous stirred tank reactor as the time and volume increments approach zero.  
(¶ 0036)

Flanagan does not disclose the use of a plug flow reactor as recited in the claims. The CSTR system that the Flanagan reactor is designed to emulate is very different from plug flow reactor. An ideal CSTR has complete back-mixing and the concentration of reactants and products are uniform throughout the reactor. By contrast, a plug flow reactor the fluid flow ideally has minimal mixing in the direction of the flow between the inlet and the outlet, i.e. the direction parallel to the overall direction of flow of the reactor.

Since Flanagan fails to disclose the use of a plug flow reactor, this reference does not provide all of the elements of the claimed invention. The § 102 rejection based on Flanagan should, therefore, be withdrawn.

*Rejection of claim 1, 2, and 8-12*

Claims 1, 2, and 8-12 stand rejected under U.S.C. § 102(e) as being anticipated by Bergh et al. (2002/0170976). The Examiner asserts that Berg teaches all of the elements of claimed invention. Applicants respectfully traverse this rejection.

Berg describes a parallel reaction system having the ability to simultaneously and independently vary temperature between separate channels. (§ 0009) The parallel reaction system includes four or more reactors and a fluid distribution system. (§ 0010) The reactors each comprise a surface defining a reaction cavity, for performing a chemical reaction, and an inlet port and an outlet port, both connected to the reaction cavity. (§ 0010) The temperature of each of the four or more reaction vessels is simultaneously and independently controlled using separately-controlled heating elements. (§ 0010) The system thus provides for temperature differences between spatially adjacent reactors.

Although Berg describes the reactor as “analogous” to a plug flow reactor, in the Berg system the products are separated by space not time, i.e. they are all made at the same time, and thus it is not a true plug flow reactor, which allows for samples to be continuously and sequentially made with different starting materials or under different processing conditions even though the samples may not be physically separated. Thus, even if one or more plug flow reactors are used in the Berg system, the system as a whole is not being used to generate a combinatorial library in a plug flow manner. For this reason, Applicants submit that Berg does not disclose all of the elements of the claimed invention. The § 102 rejection based on Berg should, therefore, be withdrawn.

### **§ 103 Rejections**

#### *Claim 14*

Claim 14 stands rejected under 35 U.S.C §103(a) as being unpatentable over Freitag et al. (U.S. Patent No. 6,566,461) in view of Citron et al. (US 2002/0026016). The Examiner asserts that Freitag describes every element of the method of claim 14, except for the use of a metallocene catalyst, and that Citron provides this missing teaching. However, as explained above Freitag does not teach all the elements of the present invention, because it fails to describe the use of a plug flow reactor. Citron does not compensate for the deficiencies of the Freitag. Thus, even in combination these references do not disclose all of the elements of claim 14. This rejection should, therefore, be withdrawn.

*Claims 5 and 7*

Claims 5 and 7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Freitag et al. (U.S. Patent No. 6,566,461) in view of Priddy et al. (U.S. Patent No. 4,572,819). The Examiner asserts that Freitag describes each and every element of the methods of claims 5 and 7, except for the use of an extruder in the reaction, and that Priddy provides this missing teaching. However, as explained above, Freitag does not disclose all of the elements of the present invention, because it fails to teach the use of a plug flow reactor. Priddy does describe the use of plug flow reactor, and thus does not compensate for the deficiencies of Freitag. Moreover, although Priddy describes the use of an extruder in making a polymer, Priddy does not use an extruder as a reactor, but only as a conveying mechanism. Thus, even in combination, these references do not disclose all of the elements of claims 5 and 7. This rejection should, therefore, be withdrawn.

*Claim 6*

Claim 6 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Freitag et al. (U.S. Patent No. 6,566,461) in view of Austin et al. (US 2002/0099137). The Examiner asserts that Freitag describes each and every element of the methods of claim 6, except for the use of a static mixture, and that Austin provides this missing teaching. However, as explained above, Freitag does not teach all the elements of the present invention, because it fails to describe the use of a plug flow reactor. Austin does not provide this teaching that is lacking from Freitag. Thus, even in combination these references do not disclose all of the elements of claim 6. This rejection should, therefore, be withdrawn.

**Conclusion**

In view of the foregoing amendments and remarks, Applicants respectfully submit that the application is in condition for allowance. Reconsideration of the application is requested.

All communications in this case should be direct to the undersigned. If the Examiner believes a telephone discussion would be helpful to resolve any of the outstanding issue in this case, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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Date

By: Sean J. Edman

Sean J. Edman, Reg. No.: 42,506

Telephone No.: (651) 575-1796

Office of Intellectual Property Counsel  
3M Innovative Properties Company  
Facsimile No.: 651-736-3833